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TOWNSEND and TOWNSEND and CREW LLP

By: /Terrie J. Rau/

PATENT
Attorney Docket No. 080306-000100US
Client Ref. No. P16809

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Ralph Mocikat

Application No.: 10/716,580

Filed: November 18, 2003

For: EXPRESSION OF IMMUNOGLOBULIN-CYTOKINE FUSION PROTEINS IN MALIGNANT B CELLS

Customer No.: 20350

Confirmation No. 6256

Examiner: WOODWARD, Cherie Michelle

Technology Center/Art Unit: 1647

APPELLANT'S REPLY BRIEF UNDER 37 C.F.R. §41.41

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
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Sir:

This brief is filed pursuant to 37 C.F.R. §41.41, in response to the Examiner's Answer mailed December 4, 2009. A Request for an Oral Hearing is NOT filed.

I. The Written Description Rejection

Claims 1-5, 7-9, and 11-17 stand rejected under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. Appellant contends that the rejection is in error because the Examiner has incorrectly applied case law incompatible with the fact pattern of this application and has failed to show why a person of ordinary skill in the art would not reasonably conclude that the present inventor had in his possession the claimed subject matter.

To reiterate, the written description requirement mandates that a patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time of filing. The pending claims of this application are drawn to a recombination vector for expressing immunoglobulin-cytokine fusion proteins in malignant B cells. The vector comprises the following components operably linked to each other: (a) a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron; (b) at least one DNA sequence encoding a constant region of an immunoglobulin or a part of the constant region; (c) a DNA sequence encoding a cytokine; and (d) a marker gene that is selectable in eukaryotic B cells and contains a functional enhancer region. In other words, one must have possession of components (a) - (d) in order to have possession of the claimed recombination vector.

In making and maintaining the written description rejection, the Examiner insists that the written description requirement is not met because the specification does not provides a sufficient number of representative species for each genus: vectors encoding cytokine-immunoglobulin fusion proteins; immunoglobulins; cytokines; marker genes; enhancers; nucleic acids homologous to a region comprising the Cμ or Cκ enhancer; bacterially compatible regulatory units; human immunoglobulin chains; interleukins; interferons; colony-stimulating factors; lymphokines; and growth factors. See pages 10-11 of the Office Action mailed March 5, 2007; pages 3-4 of the Office

Action mailed October 18, 2007; pages 3-5 of the Office Action mailed April 3, 2008; and pages 4-5 of the Final Office Action mailed January 6, 2009.

To counter the rejection, Appellant has consistently taken the position that, at the effective filing date of this application, components (a) – (d) of the claimed vector--μ or k intron sequences, immunoglobulin constant region sequences, cytokine sequences, selectable marker sequences, and enhancer sequences, were well known and available to a person of ordinary skill in the art. An artisan upon reading the present disclosure would therefore reasonably conclude that the inventor had in his possession these components and therefore the claimed vector. Appellant thus concludes that the present disclosure in fact meets the written description requirement under 35 U.S.C. §112, first paragraph.

Because these genera of components of the claimed vector and their species are well known, whether or not any representative number of species in each genus is provided in the specification is irrelevant to the question of written description. This important point distinguishes the fact pattern of this application from the case law of *Rochester* and *Kubin*, where the genera in question were not known before, containing new and previously undescribed species. Simply put, the Examiner's reliance on the case law is misplaced as important factual distinctions are not taken into consideration.

The Examiner argues, on page 5, lines 4-5, of the Examiner's Answer, that "possession of the Oxford English Dictionary does not mean that a skilled artisan can pick and choose known words to create the Collected Works of William Shakespeare." Appellant will not address this argument because this is an inappropriate analogy apparently based on the confusion between patentable subject matter and copyrightable subject matter.

The Examiner's Answer also seems to raise arguments for the written description rejection on new grounds never discussed before. the Examiner argues that, because the claimed vector comprises a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron, a "skilled artisan

would not be apprised that Appellant was in possession of a generic homologous region of a genus of κ introns without knowing something more about the structure of the homologous region required for the vector." See page 6, the first full paragraph, of the Examiner's Answer.

Appellant contends that it is highly inappropriate for the Examiner to present arguments based on a new ground in the Examiner's Answer ***for the first time*** to support the written description rejection. Because the previous three Office Actions and one Final Office Action had never discussed the question of "homologous," Appellant was never put on any notice that this question would be of any relevance to the written description assessment. Appellant had therefore made no attempt to address this specific concern during prosecution or even in the Appeal Brief.

This new ground for written description rejection is now raised well after prosecution was already closed, leaving the only chance for Appellant to address this particular basis of the written description rejection to this Reply Brief. Raising a new ground for a rejection at this late stage of appeal is utterly unfair to Appellant, who has been effectively deprived of the opportunities normally afforded to a patent applicant to address a specific concern voiced by an examiner, including multiple rounds of written communication with the Examiner, telephonic or in-person interviews, and the use of various types of evidence such as publications and expert's declarations. Indeed, it is the PTO's established policy that at the appeal stage neither the examiner nor the applicant is permitted to introduce new evidence or new grounds of arguments not already made of record. This policy precludes the use of the "homologous" argument in the Examiner's Answer to support the written description rejection. Appellant will therefore not address this particular argument in this Reply Brief.

In summary, to maintain the written description rejection is to take the position that a skilled artisan would not believe the present inventor had in his possession the claimed recombination vector, even though the components of the vector were known

in the art at the effective filing date of this application. There is no sound basis for this position. Appellant therefore respectfully requests the reversal of the written description rejection under 35 U.S.C. §112, first paragraph.

II. The Anticipation Rejection by Polack as Evidenced by Mucke

Claims 1-5, 7-9, 11, 13-17, and 29 stand rejected under 35 U.S.C. §102(e) for alleged anticipation by the Polack reference as evidenced by the Mucke reference. Appellant contends that this rejection is in error, because neither reference provides each and every limitation of the pending claims.

The Polack reference and Mucke reference describe expression vectors that contain a promoter as well as a polynucleotide sequence encoding a polypeptide to be expressed from the vectors. The limitation of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" cannot be found in either of the two references. As the Examiner has acknowledged, Polack describes the combined use of two enhancer κ intron elements, which provide a combined length of over 1.5 kb but each element is less than 1.5 kb, see, *e.g.*, the first full paragraph on page 10 and on page 20 of the Examiner's Answer. Nonetheless, the Examiner insists on reading the limitation of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" to encompass two non-continuous regions of a combined length of at least 1.5 kb. This is an unreasonable reading of the claim limitation.

As any person of ordinary skill in the art would understand, a successful recombination event requires the presence of a polynucleotide sequence that is of a continuous minimal length and homologous to the target insertion region. The specification explicitly states, on page 10, lines 20-22, that the "homologous sequence contained in said vector must have a length of at least 1.5 kb to achieve a homologous recombination event at all." This statement unequivocally conveys to an artisan that

recombination requires a minimal length of 1.5 kb for one single homologous sequence, not some combined length of a multiplicity of fragments as suggested by the Examiner.

If one were to follow the Examiner's logic and construe the limitation "a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" to cover two or more homologous fragments having some homology to the μ or κ intron, one would then find the limitation met by virtually ***any*** polynucleotide sequence greater than 1.5 kb in length, since the homologous fragments as suggested by the Examiner could be as small as a single nucleotide, which will always find homology in a target sequence.

In other words, the Examiner's claim construction of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" to read on two or more discontinuous sequences whose combined length is greater than the 1.5 kb minimal length, contradicts the very basis of the present invention and would render this claim limitation completely meaningless. This reading as proposed by the Examiner is therefore impermissible.

Taken together, the cited references fail to provide the limitation of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron," and there is no basis for the anticipation rejection. Appellant therefore respectfully submits that the rejection under 35 U.S.C. §102(e) is improper and must be reversed.

III. The Obviousness Rejection over Polack, Levy, and Gillies as Evidenced by Mucke

Claims 1-5, 7-9, 11-13, and 15-17 stand rejected under 35 U.S.C. §103 for alleged obviousness over Polack (evidenced by Mucke) in view of the Levy reference and the Gillies reference. Appellant contends that this rejection is in error, because the

cited references together fail to provide each and every limitation of the pending claims and a *prima facie* showing of obviousness is therefore not made.

In order to establish a *prima facie* case of obviousness, the cited references together must provide each and every claim limitation. As discussed in Section II, the primary reference by Polack (as evidenced by Mucke) fails to provide the claim limitation of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the κ intron," according to the proper claim construction. Neither has the Examiner identified anything in the secondary references by Levy and Gillies that apparently supplements this limitation. As such, no *prima facie* obviousness is established.

Accordingly, Appellant respectfully requests the reversal of the obviousness rejection under 35 U.S.C. §103 over Polack (evidenced by Mucke) in view of Levy and Gillies.

IV. The Obviousness Rejection over Polack, Mucke, and Mocikat

Claims 1-5, 7-9, and 11-17 stand rejected under 35 U.S.C. §103 for alleged obviousness over Polack or Mucke in view of the Mocikat reference. Appellant contends that this rejection is in error, because the Examiner has not identified any motivation for combining the cited references, nor has a reasonable expectation of success been established in combining the teaching. In the alternative, the cited references together fail to provide each and every limitation of the pending claims. A *prima facie* showing of obviousness is therefore not made.

As discussed in Section II, the primary references by Polack *et al.* and Mucke *et al.* relate to expression vectors and fail to provide at least one limitation of the pending claims, namely "a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron." The secondary reference by Mocikat is cited to provide teaching of a vector for homologous recombination at the Ig

locus. In the Final Office Action of January 6, 2009, the Examiner seems to argue that, since Mocikat *et al.* used a 2.3 kb fragment of the mouse μ intron sequence in their recombination vector, the claim limitation "a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" would be supplemented. The Examiner further argues that Mocikat provides a motivation to combine its teaching with that of Polack, because Mocikat allegedly teaches various advantageous features of this 2.3 kb mouse μ intron fragment (see pages 11 to 12 of the Final Office Action).

Appellant has addressed this specific basis for the obviousness rejection in the Appeal Brief, pointing out that there would be no motivation to combine Polack and Mocikat, due to the fundamental differences between the Polack vector (a conventional expression vector) and the Mocikat vector (an integration vector) in their purpose and mechanism of action. Appellant has also pointed out that the cited references tend to teach away from introducing the feature of 2.3 kb mouse μ intron fragment from Mocikat into the Polack vector, since it would render the Polack vector much less effective or even useless. Appellant thus reaches the conclusion that no motivation to combine has been identified and consequently no *prima facie* showing obviousness has been made.

In the Examiner's Answer, however, the Examiner has seemingly changed her arguments and now states that the central issue is whether the limitation "a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" should be read to cover two κ fragments each less than 1.5 kb in length but combinedly more than 1.5 kb (see, *e.g.*, the first full paragraph on page 20 of the Examiner's Answer). In the meantime the Examiner indicates that Mocikat is cited to provide the limitation of "a DNA sequence encoding the constant region or a part of the constant region from a mouse immunoglobulin," pertinent to dependent claim 12 only (see, *e.g.*, the bottom of page 15 to top of page 16, and the middle paragraph on page 25 of the Examiner's Answer).

Since the question of how the limitation of "a continuous region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the κ intron" should be properly construed has already been fully addressed in Section II, Appellant reiterates here that this limitation is not found in Polack/Mucke; if Mocikat is cited for providing the limitations of claim 12 only, then Mocikat does not supplement the missing limitation either. As such, no *prima facie* obviousness can be established based on the combination of Polack/Mucke and Mocikat.

Appellant therefore requests the reversal of the obviousness rejection under 35 U.S.C. §103 over Polack/Mucke in view of Mocikat.

V. Conclusion

In view of the foregoing, Appellant respectfully requests that the written description rejection under 35 U.S.C. §112, first paragraph, anticipation rejection under 35 U.S.C. §102(e), and obviousness rejections under 35 U.S.C. §103(a) be reversed.

Respectfully submitted,

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